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**From:** Calvin Willhite <[REDACTED] Ex. 6 Personal Privacy (PP)>  
**Sent:** 4/5/2021 3:47:38 PM  
**To:** Cohen, Samuel M [scohen@unmc.edu]; Allan H. SMITH [ahsmith@berkeley.edu]; tsujij@exponent.com; Harvey Clewell [hclewell@ramboll.com]; Shao, Kan [kshao@indiana.edu]; Bette Meek [bmeek@uottawa.ca]; Michael Dourson [REDACTED] Ex. 6 Personal Privacy (PP) ]; Lee, Janice [Lee.JaniceS@epa.gov]; Thayer, Kris [thayer.kris@epa.gov]; Orme-Zavaleta, Jennifer [Orme-Zavaleta.Jennifer@epa.gov]  
**Subject:** Re: SOT Arsenic Symposium

OK! This sort of thing is just what is interesting to the Symposium audience. I've asked Drs. Dourson and Meek to keep track of the various email info as this is great fodder for the Q&A.

The main problem for many of the SOT sessions is that they are boring and turgid - unless a person is working directly on a grant application for the particular subject. Here we have all the elements for a 60 Minutes piece.

If you have an interest (you have no doubt plenty of other things to do), I could send you my Patty's manuscript on Aluminum (of all things). Is aluminum boring and turgid? Not if you add dimension and color.

Same with As.

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**From:** Cohen, Samuel M <scohen@unmc.edu>  
**Sent:** Monday, April 5, 2021 8:38 AM  
**To:** Calvin Willhite <[REDACTED] Ex. 6 Personal Privacy (PP)>; Allan H. SMITH <ahsmith@berkeley.edu>; Joyce Tsuji <tsujij@exponent.com>; Harvey Clewell <HCllewell@ramboll.com>; Shao, Kan <kshao@indiana.edu>; Bette Meek <bmeek@uottawa.ca>; Michael Dourson [REDACTED] Ex. 6 Personal Privacy (PP) ]; Lee, Janice <Lee.JaniceS@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>  
**Subject:** RE: SOT Arsenic Symposium

It's poor articles like this one that distort the literature. I focused on the arsenic area, but some of the statements pertain to the other metals as well.

Many of the studies reported are in vitro and involve concentrations that are cytotoxic or even lethal in the whole organism. The role of oxidative damage is highly questionable, again is based largely on in vitro studies at high concentrations. Metalloproteinases (MP) are increased with metals, not as a sign of oxidative damage but as the way organisms handle metals to get them out of the body. The metal or metalloid replaces the zinc in the MP. Statements that arsenic and these other metals deplete glutathione are nonsense since glutathione in cells is present in millimolar concentrations whereas the metals are present at low micromolar concentrations even at acutely toxic doses. The studies they refer to on the direct effects on neural cells, mostly glial cells, are mostly in vitro where you do not have the blood brain barrier and are generally at high concentrations. Their references to the epidemiology rightly emphasizes hypertension, but forgets that essential hypertension tends to be familial, and they completely ignore the role of salt. You know there is a lot of salt in a meal when you can taste the salt in an Indian meal over the spices. Salt intake in India is very high and they have a very high incidence of CVD and hypertension. In addition, this paper does not deal at all with alternative explanations of findings or studies on alternative MOA or findings. Their statements regarding metabolism of arsenic are antiquated and no longer valid.

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**From:** Calvin Willhite <[REDACTED] Ex. 6 Personal Privacy (PP)>  
**Sent:** Saturday, April 03, 2021 2:50 PM

**To:** Allan H. SMITH <ahsmith@berkeley.edu>; Joyce Tsuji <tsujij@exponent.com>; Harvey Clewell <HClewell@ramboll.com>; Cohen, Samuel M <scohen@unmc.edu>; Shao, Kan <kshao@indiana.edu>; Bette Meek <bmeek@uottawa.ca>; Michael Dourson [Ex. 6 Personal Privacy (PP)] Lee, Janice <Lee.JaniceS@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Orme-Zavaleta, Jennifer <Orme-Zavaleta.Jennifer@epa.gov>  
**Subject:** SOT Arsenic Symposium

Non-UNMC email

I don't know that I can endorse the attached human health observations on arsenic, but if true we can now add dementia to the long list of adverse health outcomes. This comes as very bad news. Dr. Tsuji will cover cardiovascular aspects of chronic arsenic intoxication. From the attached it appears there are multiple MOAs and multiple target organs in addition to its inhibition of sulfhydryl enzymes.

One focus of the proposed Symposium is not only the shape(s) of the low-dose aspects of arsenic of which there appear to be many, but also which of the many different adverse outcomes should drive the As health risk assessment.

Hopefully Program Committee will see the importance of the problem.

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